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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/423,683	03/20/2000	MICHAEL ANTHONY CAWTHORNE	00537/163002	7045

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EXAMINER	
MOHAMED, ABDEL A	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 02/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/423,683	CAWTHORNE ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32,34,35,38,40,41,44,46,47,50,52 and 53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32,34,35,38,40,41,44,46,47,50,52 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/23/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/23/04 has been entered.

ACKNOWLEDGMENT OF AMENDMENT, REMARKS, TD, IDS AND STATUS OF THE CLAIMS

2. The amendment, remarks, terminal disclaimer (TD), information disclosure statement and Form PTO-1449 filed 11/23/04 are acknowledged, entered and considered. In view of Applicants request claims 32, 34, 35, 38, 40, 41, 44, 46, 47, 50, 52 and 53 have been amended. Claims 32, 34, 35, 38, 40, 41, 44, 46, 47, 50, 52 and 53 are now pending in the application. The rejections under 35 U.S.C. 112, second paragraph and the obviousness type double patenting are withdrawn in view of Applicant's amendment, remarks and filing of TD. Applicant's amendment and remarks with respect the rejection under 35 U.S.C. 103(a) over the prior art of record have been considered but deemed to be moot in view of the new ground of rejection necessitated by Applicant's amendment.

NEW GROUNDS OF REJECTIONS

CLAIMS REJECTION-35 U.S.C. § 102(b)

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 32, 34, 35, 38, 40, 41, 44, 46, 47, 50, 52 and 53 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 96/35950.

The reference of WO 96/35950 discloses a pharmaceutical composition comprising ligands selective for somatostatin type-5 receptor agonist (SSTR-5), which is effective in treating hyperamylinemia in a patient (see e.g. Summary of the Invention). On page 4, lines 26-37, the reference defines SSTR-5 agonist by stating what is meant by "SSTR-5 agonist" or, in the claims, "a somatostatin type-5 receptor agonist" is a compound which (i) is more selective for SSTR-5 than for SSTR-2, i.e., its K_i for SSTR-5 is lower than that for SSTR-2 (i.e., has a higher binding affinity); and (ii) inhibits the release of amylin from pancreas cells induced by an amylin release stimulator. On pages 5-6, the reference discloses the effective amount of the pharmaceutical formulation of the compound and on page 7, the reference states that a preferred SSTR-5 agonist has at least 3 times less than its K_i for SSTR-2 receptor, and more preferred SSTR-5 agonist has10 times less than its K_i for SSTR-2 receptor.

On page 12, the reference discloses the compound BIM-23052 which is the same as the compound disclosed on Table I, page 16 of the instant specification. Table I of the prior art on page 14 shows the respective ratios of the K_i's on compound BIM-23052 for the rat SSTR-2 and the K_i's for SSTR-5 to be 8.04 for SSTR-2 and 3.16 for SSTR-5 while in the instant specification on Table I of page 16 shows the K_i values for the same compound (i.e., BIM-23052) to be 11.96 for SSTR-2 and 1.22 for SSTR-5. Although, the desired activities are not defined, the prior art uses the same compound as the claimed one. Thus, the limitations requiring a higher binding affinity (i.e., K_i) for SSTR-5 than for either SSTR-1, SSTR-2, SSTR-3 or SSTR-4, these limitations are considered as functional limitations which is inherent in a composition claim, as such no probative weight is given to the claimed formulation/composition claims because the reference clearly teaches the use of the same composition.

The reference does not disclose the use of pharmaceutical composition for treating hyperlipidemia or lowering triacylglycerols, glycerols and cholesterols in the blood of a patient. Although, reference discloses a pharmaceutical composition for treatment of hyperamylinemia comprising an effective amount of a somatostatin type-5 receptor selective agonist (SSTR-5 agonist); however, a statement of usefulness or contemplated use of a claimed compound or composition in a claim is usually given little weight in distinguishing over the prior art. *In re Maeder et al.* (CCPA 1964) 337 F2d 875, 143 USPQ 248; *In re Riden et al.* (CCPA 1963) 318 F2d 761, 138 USPQ 112; *In re Sinex* (CCPA 1962) 309 F2d 488, 135 USPQ 302. Further, it is well established that the intended use of a compound (e.g., a polypeptide or a protein or a glycoprotein) does not

impart patentability to the compound. *In re Spada,* 911 F.2d 705, 15 USPQ2d 1655 (Fed. Cir. 1990) (The discovery of a new property or use of a previously known composition, even when that property and use are unobvious from the prior art, can not impart patentability to claims to the known composition); *In re Pearson*, 494 F.2d 1399, 1403, 181 USPQ 641, 644 (CCPA 1974) (intended use of an old composition does not render composition claims patentable); *In re Zierden*, 411 F.2d 1325, 1328, 162 USPQ 102, 104 (CCPA 1969). Thus, the prior art discloses the invention substantially as claimed, and as such, anticipates claims 32, 34, 35, 38, 40, 41, 44, 46, 47, 50, 52 and 53 as drafted.

CLAIMS REJECTION-35 U.S.C. 112 1st PARAGRAPH

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32, 34, 35, 38, 40, 41, 44, 46, 47, 50, 52 and 53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instantly claimed invention as amended is directed to a pharmaceutical composition comprising a therapeutically effective amount of an agonist selective for the somatostatin type-5 receptor and having a higher binding affinity for the somatostatin type-5 receptor than for either the somatostatin type-1, type-2, type-3 or type-4 receptor and a binding affinity (K_i) of less than 5 nM for the somatostatin type-5 receptor (independent claims 32, 38, 44, and 50); an agonist selective for the somatostatin type-5 receptor and having a higher binding affinity for the somatostatin type-5 receptor than for either the somatostatin type-1, type-2, type-3 or type-4 receptor has a K_i of less than 2 nM for the somatostatin type-5 (claims 34, 40, 46 and 52); and an agonist selective for the somatostatin type-5 receptor and having a higher binding affinity for the somatostatin type-5 receptor than for either the somatostatin type-1, type-2, type-3 or type-4 receptor has a K_i for the type-5 somatostatin receptor that is at least 10 times less than its K_i for the somatostatin type-2 receptor (claims 35, 41, 47 and 53).

However, the specification does not enable the pharmaceutical compositions as amended and claimed in the instant invention. The specification on page 16 (Table I) shows data which indicates the binding of various compounds to somatostatin receptors. Nevertheless, Applicant has provided little or no guidance beyond the mere presentation of binding of various compounds to somatostatin receptors to enable one of ordinary skill in the art for the a pharmaceutical composition comprising a therapeutically effective amount of an agonist selective for the somatostatin type-5 receptor and having a higher binding affinity for the somatostatin type-5 receptor than for either the somatostatin type-1, type-2, type-3 or type-4 receptor and a binding affinity

(K_i) of less than 5 nM for the somatostatin type-5 receptor, or an agonist selective for the somatostatin type-5 receptor and having a higher binding affinity for the somatostatin type-5 receptor than for either the somatostatin type-1, type-2, type-3 or type-4 receptor has a K_i of less than 2 nM for the somatostatin type-5, or an agonist selective for the somatostatin type-5 receptor and having a higher binding affinity for the somatostatin type-5 receptor than for either the somatostatin type-1, type-2, type-3 or type-4 receptor has a K_i for the type-5 somatostatin receptor that is at least 10 times less than its K_i for the somatostatin type-2 receptor in the manner claimed in claims 32, 34, 35, 38, 40, 41, 44, 46, 47, 50, 52 and 53. No structure function relationship has been established as currently amended and claimed. The instant specification on Table I show that for example, BIM-23272 is the least selective and the K_i values of compound BIM-23052 for hSSTR-2 is 11.96 and for hSSTR-5 is 1.22. Thus, no predictable enablement for K_i is disclosed. Therefore, the scope of the claims is not commensurate with the enablement provided by the disclosure with regard to use of various somatostatins or somatostatins agonists in the manner claimed in claims 32, 34, 35, 38, 40, 41, 44, 46, 47, 50, 52 and 53 for the following reasons:

The reference of Van Binst et al (Peptide Research, Vol. 5, No. 1, pp. 8-13, 1992) discloses backbone modification in somatostatin analogues and relation between conformation and activity. On page 8, the reference states that due to the broad spectrum of biological action, the native peptide has little therapeutic value. The question arises whether the multiple biological effects are mediated by different receptors present at these different target organs. Based on this hypothesis, synthetic

analogues could result in selectivity of action. Another factor which limits the use of the native molecule is the very short half-life time in the blood stream. Again, selectivity towards degradative enzymes could be achieved by analogues which differentiate enzymes from receptors. The reference concludes on page 12 by stating that it appears backbone modifications or isoteric replacements which do not conserve this backbone conformation result in compounds inactive as agonists of somatostatin.

Accordingly, the Examiner submits that given the teachings of the specification and the information known in the art, the question of whether one reasonably skilled in the art, based on the disclosure in the application coupled with information known in the art could make and use the presently claimed invention of claims 32, 34, 35, 38, 40, 41, 44, 46, 47, 50, 52 and 53 without undue experimentation. The effects of the claimed pharmaceutical compounds are unknown for the reasons discussed above, and as such, when this variable is added, the claimed invention becomes little more than conjecture. Moreover, without guidance, the changes which can be made in the peptide/protein structure and still maintain activity is unpredictable and the experimentation left to those skilled in the art is unnecessary and improperly, extensive and undue. See Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 927 F.2d, 1200, 18 USPQ2d 1016 (Fed. Cir. 1991) at 18 USPQ2d 1026-1027 and Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986).

Furthermore, the first paragraph of 35 U.S.C. 112 requires, inter alia, that a patent specification provide sufficient guidance to enable a person skilled in the art to make and use the claimed invention without undue experimentation. In re Vaeck, 947

F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991). While patent Applicants are not directed to disclose every species that falls within a generic claim, id. At 496, 20 USPQ2d at 1445, it is well settled that "the scope of the claims must bear a reasonable correlation to the scope of the enablement provided by the specification". In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Where practice of the full scope of the claims would require experimentation; factors to be considered in determining whether a disclosure would require undue experimentation ..... include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. In re Wands, 858 F. 2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Therefore, the scope of the claims is not commensurate with the enablement provided by the disclosure with regard to use of various somatostatins or somatostatins agonists in the manner claimed in claims 32, 34, 35, 38, 40, 41, 44, 46, 47, 50, 52 and 53. It would include those that have not been shown or taught to be useful or enabled by the disclosed method of making ad using the invention. Moreover, undue experimentation is necessary to determine if and under what conditions, the claimed invention as broadly claimed is enabled, since the use of various somatostatins or somatostatins agonists are contemplated and are encompassed as well as wide range of situations. The results desired appear to be highly dependent on all variables, the relationship of which is not clearly disclosed.

Therefore, in view of the above, there is no data or activity in the instant specification showing the establishment of structure function relationship for employing the intended use of pharmaceutical composition for treating hyperlipidemia or lowering triacylglycerols, glycerols and cholesterols in the blood of a patient in the manner claimed in the instant invention. Thus, the specification does not enable any person skilled in the art to which it pertains, or which is most nearly connected, to use the invention commensurate in scope with the claims. In the express absence of one or more examples, evidence and sufficient guidance, the skilled artisan would be faced with undue experimentation for practicing the invention.

CONCLUSION AND FUTURE CORRESPONDANCE

5. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272 0955. The examiner can normally be reached on First Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (571) 272 0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JON WEBER
SUPERVISORY PATENT EXAMINER

Mohamed/AAM
January 26, 2005